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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,340	02/17/2004	Neil S. Cutshall	60117-106	9233

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DAVIS WRIGHT TREMAINE, LLP
2600 CENTURY SQUARE
1501 FOURTH AVENUE
SEATTLE, WA 98101-1688

EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,340	CUTSHALL ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-30,43,44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

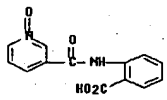
Claims 31-42 in part , drawn to method of treating wherein the compounds have R2 is a hydrogen, R3 is an aryl or an aryl alkylene as given in Group IIIa of the restriction.

The restriction is made FINAL.

Applicants have not amended the claims to the restricted and elected group.

The rejection of claims 31-42 under 35 USC 102 over Danilenko V et al still stands.

The reference discloses similar compound see RN 62833-93-6P , 62833-95-8P, 62833-97-0P as having antiphlogistic activity. (includes inflammation)



This reads on the compounds wherein n is o, R5 is H, R2 is a H and R3 is an aryl.

Claim 41 clearly state " inflammation event"

The reference teaches the compound having antiphlogistic activity. This activity included inflammation. Aaplicants specification clearly teach that theier compounds have an activity Chemokine receptor activity which includes inflammation.

On page 4 of the specifications it clearly states

" In particular, the compounds of the invention are useful for the prophylaxis and treatment of diseases or conditions involving inflammation due to neutrophil chemotaxis mediated via the CXCR1 and CXCR2 receptors. "

The rejection of claims 31-42 rejected under 35 U.S.C. 112 first para still stands.

Applicants arguments are not persuasive.

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds. With R1 being R5 or R5-(C1-C6 heteroalkylene)

2) The nature of the invention: The invention is a (highly) substituted compound that is useful to treat and inhibiting various receptors.

3) The state of the prior art: Applicants own background information on the Chemokine receptors and G-proteins indicate that they are of several types and are found in all the various cells and tissues and are of a variety of types. G-protein -coupled 7TM receptor would still be another type. The inhibiting of the various cellular events or treat the various diseases by these receptors is not an absolute predictability. The state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment of various diseases and also the IC 50 values, as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Please see article by James Cumming et al Expression and Function of Chemokine Receptors

CXCR1 and CXCR2 in Sepsis. The article clearly illustrates the complication of selecting therapeutic targets to reduce inflammation. The study clearly shows the specificity of the receptor and the disease.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high couples with the fact that applicants compounds of formula I has a very wide scope with all the various R1 and R4 groups. For e.g. the compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the R being hetero cyclic groups and also there is no data provided to show that these compounds do indeed treat various diseases. The only data provided is of 9 compounds that have an IC50 as given in **table 6** page 67, 68 of the specifications. Even this data is not consistent. The first compound does not show any CCR5 activity.! And the second last does not have any NPY1 and somat activity.!

7) The existence of working examples: The instant specification has only 9 examples with a few assays.

8) The quantity of experimentation needed to make or use the invention based on the

content of the disclosure: Since there are no working examples, and since the state of the art clearly indicates that diseases are related to very specific sub type receptors coupled with the fact that drugs have very limited predictability , the amount of experimentation is very high and burdensome and it not clear who the patient in need there of is who would require the antagonizing or inhibiting treatment since the scope of the claim is drawn to any chemokine receptor, inhibition of any chemokine mediated cellular "event" , without any indication of which patient population.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

A small scope of compounds according to the invention have been made. The assay test is noted. While these screening test in an enzyme assay provides data in certain inhibiting activity, it does not provide sufficient operational guidance in an "individual" in patho-physiological environment.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue.

"in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved"

Applicants argue that they have some examples showing the different activity and events . for example 21 provide s example of the process that is mediated by a G-protein-coupled 7TM receptor.

The table 3-5 do have data of IL-8 and GRO- α but it is not clear how the compounds could in fact treat ,

Modulate cellular "events", treat all the various disorders such as IBD, psoriasis, AIDS, cancer, artheroschlerosis, refusion injury.

Or antagonizing chemokine receptors, or

inhibiting a chemokine mediated cellular "event" or

inhibiting IL8, GRO-alpha driven neutrophil chemotaxis or

treat a disorder selected from IBD, psoriasis, AIDS, cancer, atherosclerosis, reperfusion injury or

inhibiting a G-protein –coupled , 7TM receptor or

modulate binding of Peptide YY to a NPY receptor or

modulated the binding of a somatostatin to a somatostatin cell receptor or

treat , through a therapeutically or prophalactically acceptable manner an inflammatory "event".

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
8/31/06